REMARKS

This amendment is submitted in an earnest effort to bring this case to issue without delay.

Applicant has canceled claims 13 through 19 and 21 through 24 and added new claims 26 through 39. Antecedent basis for new claims 26 through 39 may be found in the specification on pages 4 through 6 and in the specific examples. Thus claims 9 through 12, 20 and 25 through 39 are now in the application and are presented for examination.

The Examiner has rejected claims 19 through 21, 23 and 24 last presented under 35 USC 112, second paragraph, as indefinite. The Examiner refers to the terms "an otherwise healthy patient" and has indicated that he believes that this term is indefinite. The Examiner indicates that he has interpreted "an otherwise healthy patient" to mean "a patient who is healthy without taking the hormonal composition." The Examiner is more or less correct. However, to be a little more precise the term "an otherwise healthy patient" means that the patient is healthy, but for the risk of thromboembolism caused by administration of a gestagen hormone which potentially results in an elevation in plasma homocysteine levels. A particular patient within the broader definition of a healthy patient taking a gestagen hormone composition is an otherwise healthy patient from a class of individuals whose plasma homocysteine levels have been elevated by administering to the

patient a gestagen hormone composition. See the specification on page 3, lines 28 to the bottom, page 4, lines 1 through 10, and the specific examples for antecedent basis. Thus all claims now presented which define the patient as "an otherwise healthy patient" are not indefinite and no rejection of such claims should be maintained under 35 USC 112, second paragraph.

The term "otherwise healthy patient" is used throughout the relevant technical literature, including US Patents, to define particular patients receiving any number of therapies. For instance in the FERNO et al reference cited by the Examiner, page 1, paragraph 5, and page 3, paragraph 2, describes the test patients as "healthy persons" without any further explanation which indicates that the meaning of the term is well understood by those skilled in the art. Furthermore see the enclosed literature abstracts: J. Clin. Ultrasound 2005, Feb; 33(2): 63 to 66 which mentions "healthy pregnant women" as patients; Dev Med Child Neurol. 1990 Dec; 32(12) 1058 to 1060 which defines the patients as "normal children." See also Eur. J. Echocardiogr. 2005, Jul. 18 which describes treatment of a "healthy population" of patients. In addition see claim 1 of US Patent 6,562,790 which is directed to a method for abating coronary artery blockage in otherwise healthy male and female human subjects and claim 1 of US Patent 5,855,920 which is directed to a hormone replacement method comprising measuring hormone levels in a sample of an otherwise healthy human's subject blood. Accordingly there is nothing that is at all

vague and indefinite about the term "an otherwise healthy patient" used in several of the claims now presented.

The Examiner has rejected claims 9 through 13, 15, 16, 21, 22 and 25 under 35 USC 102 as anticipated by ALI et al. The Examiner maintains that the ALI et al reference encourages elderly women taking hormone replacement therapy to drink milk. Since milk contains folic acid, Vitamin $B_6$, and Vitamin $B_{12}$, the Examiner maintains that inherently when such a patient drinks milk along with taking her hormone replacement therapy, the invention as covered in the abovementioned claims is anticipated. The Examiner notes that Applicants disclose a general range for the amount of the plasma homocysteine level reducing agent administered to the patient in need of such treatment and that such a range in his opinion is broad enough to encompass administration of folic acid, Vitamin $B_6$ or Vitamin $B_{12}$ by drinking milk.

Applicant does not agree with the Examiner's interpretation of "general range." The general range of 100 micrograms to 9 grams per day of plasma homocysteine reducing agent was disclosed so broadly only because Applicant did not want to be limited in the type of plasma homocysteine reducing agent disclosed. Nowhere did Applicant say that this entire broad dosage range was applicable to each and every plasma homocysteine reducing agent and certainly did not disclose that the entire range was applicable to folic acid, Vitamin $B_6$ and Vitamin $B_{12}$. As explained in Applicant's amendment of 13 April 2005 on page 7 and in the

appeal brief on pages 12 and 13, the specific therapeutically effective dosage ranges for folic acid, Vitamin $B_6$ and Vitamin $B_{12}$ disclosed on page 6 of the application are all well above the minuscule amounts of the folic acid, Vitamin $B_6$ and Vitamin $B_{12}$ found in milk. Claims 9 through 13 and 25 rejected by the Examiner as anticipated by this reference define the amount of the plasma homocysteine reducing agent administered as a therapeutically effective amount so that the minuscule amounts of these vitamins found in milk do not fall within the scope of these claims or of any claim now presented when a patient undergoing gestagen therapy drinks a glass of milk or even a quart of milk or a gallon of milk in one day. Claims 15, 16, 21 and 22 have been canceled. Thus ALI et al is not anticipatory of any claim now presented.

In addition Applicant has submitted new claims 36 through 38 which disclose the specific dosage ranges listed in the specification on page 6, lines 25 to 30 for folic acid, Vitamin $B_6$ and Vitamin $B_{12}$, which are undoubtedly beyond the scope of the teachings of ALI et al for a patient receiving gestagen therapy for hormone replacement to drink milk. Thus claims certainly are not anticipated by ALI et al.

ALI et al provides no basis to reject any claim now presented as obvious under 35 USC 103. There is no suggestion in ALI et al that the administration of a plasma homocysteine reducing agent to a patient undergoing gestagen therapy would reduce a risk to the patient of thromboembolism induced by taking the gestagen

hormone. Furthermore there is no specific suggestion in ALI et al that administration of a plasma homocysteine reducing agent to an otherwise healthy patient receiving gestagen hormone therapy and having an elevated plasma homocysteine level as a result of administration of the gestagen hormone would have the risk of thromboembolism reduced through lowering the elevated plasma homocysteine level following administration of the plasma homocysteine reducing agent. See especially claim 33. Thus no rejection of any claim now presented should be maintained as obvious under 35 USC 103 in view of ALI et al.

The Examiner has rejected claims 19, 20, 23 and 24 under 35 USC 102 as anticipated by SPELLACY et al. The Examiner maintains that SPELLACY et al discloses administration of Vitamin $B_6$ along with progesterone as an oral contraceptive. The Examiner notes the Applicant's arguments that Applicant administers a plasma homocysteine reducing agent such as Vitamin $B_6$ to patients receiving gestagen therapy who are healthy patients except for the fact that they are at risk for thromboembolism after receiving gestagen hormone therapy because of the risk that the patient's plasma level of homocysteine will become elevated after taking the gestagen therapy. The Examiner refuses to accept that Applicant's invention is distinguishable over the SPELLACY et al disclosure for treating healthy patients since according to the Examiner Patient No. 10 listed in Table 1 is a healthy patient. Applicant disagrees.

There is no indication in SPELLACY et al that Patient No. 10 listed in Table 1 is a healthy patient. In fact the abstract of SPELLACY et al specifically states that all twelve patients showed progressively deteriorating glucose tolerance tests while taking steroid contraceptives and that all twelve patients were given Vitamin $B_6$ to treat a carbohydrate metabolism disorder associated with taking the contraceptives. Patient No. 10 started out initially on contraceptives (Steroid Treatment Test 1) with an elevated glucose level and after taking the contraceptives for six months, the glucose level actually went down (Steroid Treatment Test 2). Then when therapy commenced with Vitamin $B_6$ along with the contraceptive, Patient 10 actually experienced a slight increase in glucose blood level. This is contrary to the rest of the patients who for the most part had higher glucose levels in the blood according to Steroid Treatment Test 2 as opposed to Steroid Treatment Test 1 and had lower levels of blood glucose according to Test 3 where both Steroid and Vitamin B6 were administered than according to Test 2. Nonetheless Patient 10 still had an elevated blood glucose level according to Test 1 and is not considered by SPELLACY et al to be a healthy patient.

The whole purpose behind the SPELLACY et al disclosure is to help patients taking gestagen contraceptives who are glucose intolerant. According to SPELLACY et al administration of Vitamin $B_6$ to a patient receiving contraceptives is only taught to be of value when the patient suffers from a defect in carbohydrate

metabolism as manifested by glucose intolerance. There is no teaching in this reference to administer Vitamin $B_6$ or any other plasma homocysteine reducing agent in combination with a gestagen hormone to a patient to reduce the risk of thromboembolism caused by the gestagen hormone and especially no teaching to administer Vitamin $B_6$ in combination with a gestagen hormone to an otherwise healthy patient to prevent a risk of thromboembolism resulting from elevation of the plasma homocysteine level caused by the gestagen. Accordingly SPELLACY et al provides no basis to reject claim 19 or any other claim now presented as either anticipated under 35 USC 102 or as obvious under 35 USC 103. It is noted that claims 23 and 24 have been canceled.

In BUTTERWORTH et al the situation is similar to that of SPELLACY et al. The Examiner has rejected claims 19, 20, 23 and 24 as anticipated. In BUTTERWORTH et al female patients received a gestagen hormone for contraception and were also administered folic acid in a dosage of 10 mg/day. However, the patients did not receive the folic acid for to reduce a risk to the patient of thromboembolism induced by taking the gestagen hormone. Furthermore the patients receiving the folic acid in combination with a gestagen contraceptive were not healthy patients, but were patients suffering from dysplasia of the uterine cervix. In all claims now presented the patient is characterized as either a patient treated with a gestagen hormone in combination with a plasma homocysteine reducing agent to reduce the risk of

thromboembolism caused by the gestagen hormone or more specifically as an otherwise healthy patient receiving gestagen therapy in combination with a plasma homocysteine reducing agent to prevent a risk of thromboembolism resulting from elevation of the plasma homocysteine level caused by the gestagen. Accordingly BUTTERWORTH et al provides no basis to reject claim 20 or any other claim now presented as either anticipated under 35 USC 102 or as obvious under 35 USC 103. It is noted that claims 19, 23 and 24 have been canceled.

The Examiner has rejected claims 9 through 13, 15, 16, and 19 through 25 under 35 USC 103 as obvious citing the combination of JACKSON et al (A) and FERMO et al (R). The Examiner has cited JACKSON et al for its disclosure of providing dietary supplements to women at a variety of life stages where the supplements can contain folic acid, Vitamin $B_6$ and Vitamin $B_{12}$. JACKSON et al further discloses that these three vitamins synergistically are useful in reducing serum homocysteine levels in patients. However, as admitted by the Examiner, there is absolutely no disclosure or suggestion to administer to a patient a gestagen hormone for any purpose whatsoever, let alone for the purposes specified in the claims now presented, including contraception, hormone replacement therapy, and in conjunction with in vitro fertilization procedures, to prevent the risk of thromboembolism associated with the taking of the gestagen hormone and especially to prevent the risk of elevated plasma homocysteine levels in

otherwise healthy patients taking a gestagen hormone where the gestagen hormone may cause the elevation in plasma homocysteine levels. Thus JACKSON per se provides no basis to reject any claim now presented as obvious under 35 USC 103.

The Examiner has combined JACKSON et al with FERMO et al and notes that FERMO et al discloses that hyperhomocysteinemia is a risk factor in patients developing thrombosis. The Examiner concludes that it would be obvious from JACKSON et al to administer folic acid, Vitamin $B_6$ or Vitamin $B_{12}$ to a patient taking a gestagen hormone composition to prevent the risk of thromboembolism associated with taking the gestagen hormone in view of the disclosure in FERMO et al that elevated blood levels of homocysteine are a risk factor in thrombosis even though there is no disclosure in FERMO et al of administering folic acid, Vitamin $B_6$ or Vitamin $B_{12}$ to a patient for any purpose or of any connection between administering gestagen hormones to a patient and increased levels of plasma homocysteine. Furthermore there is no disclosure or suggestion of administering folic acid, Vitamin $B_6$ or Vitamin $B_{12}$ together with a gestagen hormone, to a patient taking a gestagen hormone composition, for the purpose of preventing a risk of thromboembolism caused by administration of the gestagen hormone composition, and more specifically to an otherwise healthy patient at risk of having an elevated plasma homocysteine level that is a result of taking the gestagen hormone composition.

Before Applicant's invention it was not known in the literature that thromboembolism induced by gestagens could be prevented by homocysteine reducing agents since not each type of thromboembolism can be prevented by folic acid (e.g. thromboembolism caused by atrial fibrillation, hypertriglyceridemia, immobilization, renal failure) and not each type of hyperhomocysteinemia can be treated by folic acid (e.g. hyperhomocysteinemia induced by renal failure). So by combining the documents cited the skilled person could not arrive at the method invented by the Applicant, namely the prevention of thromboembolism induced by gestagens by folic acid or other homocysteine reducing agents.

There is no suggestion in either reference that the administration of a gestagen hormone to a patient could increase the risk of the patient to thromboembolism, no suggestion that administration of folic acid, Vitamin $B_6$ or Vitamin $B_{12}$ to a patient in conjunction with a gestagen hormone composition would reduce the risk of the patient taking a gestagen hormone to thromboembolism, and no suggestion of administration of folic acid, Vitamin $B_6$ or Vitamin $B_{12}$ to a patient taking a gestagen hormone and at risk of having an elevated plasma homocysteine level as a result of taking the gestagen hormone, but who is an otherwise healthy patient to prevent the risk of thromboembolism. The fact that JACKSON et al discloses the administration of folic acid, Vitamin $B_6$ and Vitamin $B_{12}$ to synergistically reduce serum homocysteine

levels in patients having this condition and that FERMO et al discloses a connection between elevated blood levels of homocysteine and thrombosis falls far short of rendering obvious any claim now presented not only because there is no suggestion in the references taken individually or together to administer folic acid, Vitamin $B_6$ or Vitamin $B_{12}$ together with the gestagen hormone for any purpose, but also because there is no disclosure or suggestion in either reference that there is any connection between the administration of a gestagen hormone to an otherwise healthy patient, and increased risk of thromboembolism, where the otherwise healthy patient has or may have elevated plasma homocysteine levels as a result of taking the gestagen hormone composition. Thus no rejection of any claim now presented should be maintained under 35 USC 103 in view of this combination of references. It is noted that claims 15, 16, 19 and 21 through 24 have been canceled.

The Examiner has rejected claims 9 through 11, 13, and 15 through 24 under 35 USC 102(e) as anticipated by KAFRISSEN et al (B). The Examiner contends that this reference discloses a method of administering folic acid along with oral contraceptives containing progesterone or hormone replacement therapy containing progesterone. The Examiner also notes that the reference discloses that the amount of folic acid administered to the patient ranges between 25 μg and 1g to reduce blood levels of homocysteine.

Applicant does not agree that KAFRISSEN et al is anticipatory of any claim now presented. The patients treated

according to KAFRISSEN et al are not the same patients, treated according to the presently claimed methods, who are taking the plasma homocysteine reducing agent to reduce a risk to the patient of thromboembolism induced by taking the gestagen hormone and are definitely not otherwise healthy patients who are taking the plasma homocysteine reducing agent to reduce a risk to the patient of thromboembolism induced by taking the gestagen hormone, and most definitely are not the otherwise healthy patients having or who may have an elevated plasma homocysteine level resulting from taking a gestagen hormone. The reason why is that KAFRISSEN et al defines the patient treated as follows: "the subject is from a population whose members are afflicted with or predisposed to become afflicted with, a disorder at a higher than normal incidence." See claim 1, part (b). Therefore it is understood that the KAFRISSEN et al patients are either ill, or they have a risk factor (i.e. abnormality) before taking the gestagen hormone. In other words, the patient's risk factor is not due to taking the gestagen hormone. The term "higher than normal incidence" means that the incidence of some diseases and/or of some risk factors (disorders) in that population is higher than the incidence in a healthy population. In connection with folic acid administration, Applicant's invention was to realize that folic acid administration together with gestagen is recommended for a healthy population in contrast to the KAFRISSEN et al disclosure where the method of treatment disclosed therein is strictly recommended only for "a

population whose members are afflicted with, or predisposed to become afflicted with, a disorder at a higher-than-normal incidence." Thus the presently claimed invention is patentably distinguishable from the KAFRISSEN et al disclosure.

Apart from KAFRISSEN et al which discloses the treatment of those whose members are afflicted with, or predisposed to become afflicted with, a disorder at a higher-than-normal incidence. In fact the healthy patients treated according to the Applicant's presently claimed invention are the same kind of patient as one from a population whose members are afflicted with, or predisposed to become afflicted with, a disoreder at a normal incidence, and in this sense those patients are exactly those not covered by KAFRISSEN et al. Such patients are the kinds of patients disclosed in the abstracts cited earlier in this amendment: J. Clin. Ultrasound 2005, Feb; 33(2): 63 to 66 defining the patients as healthy pregnant women; Dev Med Child Neurol. 1990 Dec; 32(12) 1058 to 1060 defining the patients as normal children; and Eur. J. Echocardiogr. 2005, Jul. 18 describing treatment of a healthy population of patients. In other words, the term "normal incidence" refers to the group of healthy patients, and, consequently, the term "higher than normal incidence" refers to the group of non-healthy patients. Therefore, the group of patients for whom KAFRISSEN et al recommends their method strictly differs from the population treated according to the presently claimed method.

It is not at all obvious that a treatment suggested for a certain population (i.e. a population whose members are afflicted with, or predisposed to become afflicted with, a disorder at a higher-than-normal incidence") would automatically be suggested also to healthy patients, since for example, extended folic acid administration has a number of side effects (e.g. increased appetite, then obesity, and its detrimental effects; possible acceleration of the growth of certain tumors. In view of the above Applicant maintains that the KAFRISSEN et al reference provides no basis to reject any claim now presented as anticipated under 35 USC 102(e) or 35 USC 103.

Applicants emphasize that claims 10, 12, 25, 26, 28, 29, 30, 31, 37, and 38 do not include folic acid among the plasma homocysteine reducing agents. Accordingly KAFRISSEN et al is especially believed to be far removed from those claims and provides no basis to reject any of those claims under 35 USC 102 or 103.

Applicant notes that the issue date of KAFRISSEN et al is 20 February 2001 after Applicant's International Filing Date of 28 January 2000 and long after Applicant's Hungarian priority date of 1 February 1999. Applicant further notes that the effective date of KAFRISSEN et al as a reference under 35 USC 102(e) is 17 April 1998, the filing date of US Provisional Application 60/082,068. Applicant began his experimentation in 1995 in which experiments were conducted on patients receiving gestagen therapy

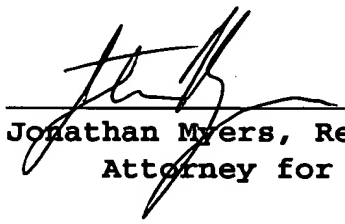
and a plasma homocysteine reducing agent. Applicant initially conceived of his invention in Europe on 3 June 1996 and over the next couple of years diligently reduced his invention to practice. Applicant is enclosing a Declaration Under 37 CFR 1.131 with attachments to establish that his date of first experimentation, his date of conception, and his date of constructive reduction to practice. It is noted that he began experimentation and conceived of his invention well before the effective date of KAFRISSEN et al as a reference.

Thus not only is the KAFRISSEN et al reference not a basis to reject any claim now presented under either 35 USC 102(e) or 103, but furthermore Applicant has submitted a Declaration Under 37 CFR 1.131 to swear back of the reference so that the reference is no longer an effective reference in this application.

During the prosecution of the parallel European Patent Application, the European Patent Office cited WO 00/51596 as relevant prior art. The reference is in French and no English translation is available to the Applicant. Furthermore under US law the effective date of this publication as a reference is its publication date of 8 September 2000 which is not only subsequent to the Applicant's Hungarian priority date of 1 February 1999, but is subsequent to the Applicant's International Filing Date of 28 January 2000. Accordingly the reference is not an effective reference against any claim in this application.

Applicant believes that all claims now presented are in condition for allowance and a response to that effect is earnestly solicited. Applicant encloses a petition to obtain a one month extension of the term for response and authorization is enclosed for payment for the petition to be charged to the credit card of the undersigned attorneys by submission of PTO-2038 (small entity).

Respectfully submitted,
The Firm of Karl F. Ross P.C.



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Enclosures: Declaration Under 37 CFR 1.131 with
Attachments A, B, B1, C, C1, D and D1
Petition for Extension
PTO-2038
5 References
WO 00/51596